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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/142,597	03/05/1999	WILLIAM BUTLER COWDEN	120081.403	2400

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	18

DATE MAILED: 04/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/142,597	Cowden et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 17, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 6-8, 15-17, and 19-21* is/~~are~~ pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6-8, 15-17, and 19-21* is/~~are~~ rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11.*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 01/17/02 (paper no. 15) has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 01/17/02 (paper no. 16) in response to the final Office Action mailed 03/21/01 (paper no. 10).

Status of Claims

3) Claims 1 and 15 have been amended via the amendment filed 01/28/02.

Claims 1-4, 6-8, 15-17 and 19-21 are pending and are under examination.

The Cowden Declaration under 37 CFR 1.132

4) Acknowledgment is made of Applicants' submission of the Cowden Declaration filed 01/17/02 (paper no. 17).

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Maintained

7) The rejection of 1-4, 6-8, 15-17 and 19-21 made in paragraph 7 of the Office Action mailed 06/21/00 (paper no. 7) and maintained in paragraph 12 of the Office Action filed 03/21/01 (paper no. 10) under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is maintained for reasons set forth therein and herebelow.

It is noted that Applicants have amended claims 1 and 15 by replacing the recitation "a species of *Coxiella*" with --non-infectious *Coxiella burnetii*--.

With regard to the scope of the broadly recited "autoimmune disease" and "one or more antigenic components", Applicants contend that "the cited references support the use of an hsp antigen of *C. burnetii* for treatment of autoimmune disease". Applicants point to a passage from an unspecified "cited reference" as allegedly teaching the alignment of "the 2-kDa" polypeptides from *C. burnetii* and *M. leprae*. Applicants assert that immune recognition of a protein is dependent upon tertiary structure and that even a single amino acid change at a critical point in a given protein can completely eliminate induction of an immun response to the protein, let alone a 45% alteration in amino acid sequence. Applicants contend that a cell-mediated immune response can be raised against certain T cell epitopes found in hsps of mycobacterial species. Applicants assert that there was no evidence for the induction of arthritis in any of the treated animals described in the present specification. Applicants state that van Eden *et al.* teach that hsp antigen actually prevented the induction of arthritis in the treated rats. Via the Cowden Declaration, Applicants submit that various fractions of *C. burnetii* are effective in the treatment of IDDM "while other fractions are without such activity". The Declaration submits that the CMR residue remaining after delipidation of whole *C. burnetii* and a DMSO extract of whole cell *C. burnetii* were effective in "inhibiting the onset of IDDM in NOD mice", whereas the components of the extracted lipidic material, CME, and the LPS fraction of *C. burnetii* are "**without** such activity" [Emphasis added].

Applicants' arguments have been carefully considered, but are non-persuasive. No mention was made of a "2-kDa" polypeptide in paragraph 12 of the Office Action mailed 03/21/01. Instead, the example of hsp was given to establish that the entire scope of "autoimmune disease" and "one or more antigenic components" is not enabled. From what is widely known in the art, it can hardly be argued that microbial HSPs are not associated with autoimmune consequences, including arthritis. Even post-filing references teach the autoimmune potential of microbial HSPs. For instance, Willis *et al.* (US 6,066,333, filed in September 1995 and issued in May 2000) disclose the following:

> ..... Immune responses to HSPs can be highly cross-reactive and even auto-reactive due to their extensive inter-species amino acid homology. Immune responses to HSPs have already been implicated in adjuvant

> arthritis in the rat, pristane arthritis in the mouse, diabetes mellitus in the non-obese diabetic mouse, rheumatoid arthritis, systemic lupus erythematosus, atherosclerosis and in human surveillance. Therefore, it appears that HSPs may have a paradoxical effect in pathological conditions, having a cyto-protective effect on cells and tissue in stressful environments, but eliciting a detrimental immune response in some autoimmune diseases.

That the entire scope of the instant claims is non-enabled is established herebelow, now using the data provided in the Declaration filed by Applicants. The Cowden Declaration renders the hsp example unnecessary by providing the *prima facie* evidence contrary to the Applicants' arguments. The Declaration establishes clearly that the entire scope of instant claims is non-enabled. The data provided therein shows that while some antigenic components of *C. burnetii* (the CMR residue and the DMSO extract) delay the onset of one specific autoimmune disease, IDDM, as observed during a period of 200 days, other antigenic components of *C. burnetii* (a CME component and the LPS fraction) did not. The Declaration further establishes that the IDDM-delaying effect of one antigenic component of *C. burnetii,* such as the CMR residue or the DMSO extract, cannot be extrapolated to another antigenic component of *C. burnetii,* such as the CME component or the LPS fraction. The inoperative antigenic components of non-infectious *Coxiella burnetii* necessarily fail to meet the how-to-use aspect of the enablement requirement of 35 U.S.C. 112, first paragraph.

Furthermore, neither the specification nor the Cowden Declaration provides any data showing that a non-infectious *Coxiella burnetii* or any of its antigenic components "prevent" the effects of IDDM or any autoimmune disease in a mammal. There is no certainty that the "membrane/wall preparation" or an "endospore preparation" of *Coxiella* sp. recited on page 6 of the specification would inhibit, prevent, ameliorate or delay the onset of IDDM or any autoimmune disease in a mammal. The Webster's II New Riverside University Dictionary (1984) defines the term "prevent" as "to keep from happening". Autoimmune diseases, including IDDM, are complex diseases involving different aetiology and mechanisms. The specification does not support a method which keeps the process of any autoimmune disease from happening in a mammal, especially beyond the study observation period of 200-300 days. Additionally, there is absolutely no evidence that a non-infectious *C. burnetii* or one or more antigenic components therefrom would inhibit, prevent, ameliorate or delay the onset of a myriad of non-IDDM autoimmune conditions that are known in the art, including those recited on page 5 of the

specification: pernicious anemia, autoimmune chronic hepatitis, ulcerative colitis, primary biliary cirrhosis, multiple sclerosis and systemic lupus erythematosus. Instant claims are viewed as not meeting the scope of enabled provisions of 35 U.S.C § 112, first paragraph. The rejection stands. Clearly, the full scope of the claims is not commensurate with the enabling disclosure. Undue experimentation would have been required at the time of the effective filing date of the instant application for one of ordinary skill in the art to reproducibly practice the full scope of the broadly claimed method "for preventing an autoimmune disease" by administering to a mammal non-infectious *Coxiella burnetii* or any of its antigenic components. The ability to reproducibly practice the full scope of the claimed method is well outside the realm of routine experimentation.

8) The rejection of claims 1, 2, 15, 16, 20 and 21 made in paragraph 12 of the Office Action mailed 06/21/00 (paper no. 7) and maintained in paragraph 13 of the Office Action mailed 03/21/01 (paper no. 10) under 35 U.S.C § 103(a) as being unpatentable over Zhang *et al.* (*Acta Virologica* 38: 327-332, 1994), or Gajdosova *et al.* (*Acta Virologica* 38: 339-344, 1994), each in view of Levy *et al.* (*Eur. J. Epidemiol.* 5: 447-453, 1989, abstract), or Roue *et al.* (*Lancet* 341: 1094-1095, 1993), is maintained for reasons set forth therein and herebelow.

Applicants contend that the claimed invention is not obvious over the cited prior art, since Zhang *et al.* and Gajdosova *et al.* do not teach a composition for preventing, inhibiting, or ameliorating an autoimmune disease in a mammal, and that neither Levy *et al.* nor Roue *et al.* remedy this deficiency. Applicants state that neither Levy *et al.* nor Roue *et al.* teach or suggest that the compositions of Zhang *et al.* or Gajdosova *et al.* would be effective in preventing or treating the effects of autoimmune diseases. Applicants assert that the findings of Levy *et al.* or Roue *et al.* do not appear particularly relevant to the claims of the instant invention. Applicants, however, acknowledge that autoimmune response "can and do occur" following a bacterial or viral infection, that "the potential for production of autoimmune phenomena following any infection is real and well noted in the medical literature" and that the "phenomenon is extremely well known in the literature". Applicants state that this phenomenon is not unique to *Coxiella* or mycobacteria or even to bacteria. Applicants provide a detailed discussion on the autoimmune disease induced by acute disseminated viral encephalomyelitis.

Applicants' arguments have been carefully considered, but are non-persuasive. The Applicants' discussion on autoimmune viral diseases does not appear to be relevant. Applicants are reminded that if Zhang *et al.*, Gajdosova *et al.*, Levy *et al.* and Roue *et al.* expressly taught the use a *Coxiella burnetii* composition in a method for preventing, inhibiting, or ameliorating an autoimmune disease in a mammal, these references would have been applied to reject the instant claims under 35 U.S.C § 102. Instead, the references are applied in a rejection under 35 U.S.C § 103. As acknowledged by Applicants, both Levy *et al.* and Roue *et al.* teach the autoimmune nature of Q fever. As set forth in paragraph 12 of the Office Action mailed 06/21/00 (paper no. 7) and paragraph 13 of the Office Action mailed 03/21/01 (paper no. 10), Zhang *et al.* or Gajdosova *et al.* teach a composition comprising a purified antigenic outer membrane protein component, phase I killed whole cells or Cb I (i.e., QFA) and/or outer membrane components of *Coxiella burnetii* contained in a pharmaceutically acceptable carrier or an adjuvant, and a method of administering the same to mammals to induce immunity and confer protection against Q fever, a disease recognized in the art as being autoimmune in nature. Q fever is viewed as inherently an autoimmune disease. The Office has clearly established a *prima facie* case of obviousness. The rejection stands.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

9) Claims 1-4, 6-8, 15-17 and 19-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 1 and 15 are vague and indefinite in the recitation: "preventing, inhibiting, ... or ameliorating" the effects of an autoimmune disease, because it is unclear what the differences are between these terms. It is not clear which symptoms or markers represent preventing, inhibiting or ameliorating effects.

(b) Claims 2-4, 6-8, 16, 17 and 19-21, which depend directly or indirectly from claims 1 and 15, are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, because of the indefiniteness or vagueness identified above in the base claims.

Relevant Prior Art

10) The prior art made of record and not relied upon currently in any rejection is considered

pertinent to Applicants' disclosure:

- Williams *et al.* (*Infect. Immun.* 51: 851-858, 1986) disclose a vaccine comprising phase I *Coxiella burnetii* chloroform-methanol residue (CMRV) which induces active immunity against Q fever in mice (see entire document).

Remarks

11) Claims 1-4, 6-8, 15-17 and 19-21 stand rejected.

12) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9306.

13) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

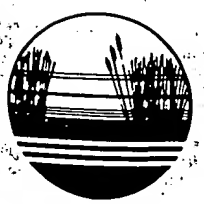
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

April 2002

S. DEVI, PH.D.
PRIMARY EXAMINER

New Riverside University Dictionary

1984



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—vail·ing (prĭ-vā'lĭng) *adj.* 1. Most frequent or common: PREDOMINANT. 2. Generally current: WIDESPREAD. **—pre·vail'ing·ly** *adv.* **—pre·vail'ing·ness** *n.*

SYNS: PREVAILING, CURRENT, PREVALENT, REGNANT, RIFE, WIDESPREAD *adj. core meaning:* most commonly existing or encountered at a given time <the *prevailing* views in astrophysics>

prev·a·lent (prĕv'ə-lənt) *adj.* [Lat. *praevalens, praevalent-*, pr.part. of *praevalere*, to be stronger. —see PREVAIL.] Widely existing, accepted, or practiced. **—prev'a·lence** *n.* **—prev'a·lent·ly** *adv.*

pre·var·i·cate (prĭ-văr'ĭ-kāt') *vi.* **-cat·ed, -cat·ing, -cates.** [Lat. *praevaricari, praevaricat-*, *prae-*, before + *varicare*, to straddle < *varicus*, straddling <*varus*, bent.] To stray from or evade the truth: EQUIVOCATE. **—pre·var'i·ca'tion** *n.* **—pre·var'i·ca'tor** *n.*

pre·ven·ience (prĭ-vēn'yəns) *n.* 1. The act or state of being antecedent or prevenient. 2. Attention to another's needs.

pre·ven·ient (prĭ-vēn'yənt) *adj.* [Lat. *praevenient-*, pr.part. of *praevenire*, to precede: *prae-*, before + *venire*, to come.] 1. Antecedent. 2. Anticipatory. **—pre·ven'ient·ly** *adv.*

pre·vent (prĭ-vĕnt') *v.* **-vent·ed, -vent·ing, -vents.** [ME *prevenen*, to anticipate <Lat. *praevenire*: *prae-*, before + *venire*, to come.] —*vt.* 1. To keep from happening: AVERT. 2. To keep (someone) from doing something: IMPEDE <*prevented* me from playing> 3. To anticipate or counter in advance. 4. *Archaic.* To come before: PRECEDE. —*vi.* To present an obstacle <There will be a game if nothing *prevents*.> **—pre·vent'a·bil'i·ty, pre·vent'i·bil'i·ty** *n.* **—pre·vent'a·ble, pre·vent'i·ble** *adj.* **—pre·vent'er** *n.* **—pre·ven'tion** (-vĕn'shən) *n.*

pre·ven·ta·tive (prĭ-vĕn'tə-tĭv) *adj. & n. var. of* PREVENTIVE.

pre·ven·tive (prĭ-vĕn'tĭv) *also* **pre·ven·ta·tive** (-tə-tĭv) —*adj.* 1. Intended or used to hinder or prevent. 2. *Med.* Thwarting or warding off illness or disease: PROPHYLACTIC. —*n.* 1. Something that prevents: OBSTACLE. 2. *Med.* Something for warding off illness. **—pre·ven'tive·ly** *adv.* **—pre·ven'tive·ness** *n.*

preventive detention *n.* Pretrial imprisonment without the right to bail of one accused of a felony and judged dangerous to society.

pre·view *also* **pre·vue** (prē'vyōō') —*n.* 1. An advance showing, as of a film, to an invited audience before public presentation. 2. An advance viewing or exhibition, esp. the presentation of several scenes advertising a forthcoming film. 3. An introductory or limited experience. —*vt.* **-viewed, -view·ing, -views** *also* **-vued, -vu·ing, -vues.** To exhibit or view in advance.

pre·vi·ous (prē'vē-əs) *adj.* [Lat. *praevius*, going before *prae-*, before + *via*, way.] 1. Existing or happening prior to something else in time or order: ANTECEDENT. 2. *Informal.* Hasty: premature. **—pre'vi·ous·ly** *adv.* **—pre'vi·ous·ness** *n.*

previous question *n.* The motion in parliamentary procedure to take an immediate vote on the main question under consideration or on any other questions so designated.

previous to *prep.* Prior to: BEFORE.

pre·vise (prĭ-vīz') *vt.* **-vised, -vis·ing, -vis·es.** [Lat. *praevidēre*, *praevis-*: *prae-*, before + *vidēre*, to see.] To foresee. 2. To notify ahead of time. **—pre·vi'sion** (-vĭzh'ən) *n.* **—pre·vi'sion·al, pre·vi'sion·ar'y** (-ə-nĕr'ē) *adj.* **—pre·vi'sor** *n.*

pre·vo·cal·ic (prē'vō-kăl'ĭk) *adj.* Coming before a vowel.

pre·vo·ca·tion·al (prē'vō-kā'shə-nəl) *adj.* Of or relating to instruction given in preparation for vocational school.

pre·vue (prē'vyōō') *n. & v. var. of* PREVIEW.

pre-war (prē'wôr') *adj.* Existing or taking place before a war.

prex·y (prĕk'sē) *n., pl.* **-ies.** [Shortening and alteration of PRESIDENT.] *Slang.* A president, esp. of a college or university.

prey (prā) *n.* [ME *preie* < OFr. < Lat. *praeda*.] 1. A creature hunted or caught for food: QUARRY. 2. A victim. 3. An act of preying. —*vi.* **preyed, prey·ing, preys.** 1. To hunt, catch, or eat as prey <Foxes *prey* on chickens.> 2. To victimize or make a profit at someone else's expense. 3. To plunder: pillage. 4. To exert a baneful or injurious effect <Guilt *preyed* upon my mind.> **—prey'er** *n.*

Priam (prī'əm) *n.* [Lat. *Priamus* < Gk. *Priamos*.] *Gk. Myth.* King of Troy, the father of Paris and Hector, who was killed when the Greeks captured his city.

pri·a·pic (prī-ā'pĭk, -ăp'ĭk) *also* **pri·a·pe·an** (prī'ə-pē'ən) *adj.* [< PRIAPUS.] Phallic.

pri·a·pism (prī'ə-pĭz'əm) *n.* [Fr. *priapisme* < LLat. *priapismus* < Gk. *priapismos* < *priapizein*, to have an erection < *Priapos*, Priapus.] *Pathol.* A persistent, usu. painful erection of the penis, esp. due to disease.

Pri·a·pus (prī-ā'pəs) *n.* [Lat. < Gk. *Priapos*.] 1. **Priapus.** *Gk. & Rom. Myth.* The god of procreation, guardian of vineyards and gardens and personification of the erect phallus. 2. An image of Priapus, often used in ancient gardens as a scarecrow. 3. A phallic representation.

price (prīs) *n.* [ME *pris* < OFr. < Lat. *pretium*.] 1. The sum of money or goods asked or given for something. 2. The cost at which something is obtained. 3. The cost of bribing someone. 4. A reward offered for the killing or capture of a person. 5. Value: worth. —*vt.* **priced, price·ing, price·es.** 1. To set a price for <socks *priced* at $50> 2. To find out the price of <spent the day *pricing* cars> **—price out of the market.** To charge so much for goods or services that people no longer buy or use them.

price cutting *n.* Reduction of retail prices to a level so low as to eliminate competition.

price-earnings ratio (prīs'ûr'nĭngz) *n.* The ratio of a common stock's market price to its earnings per share, used as an indicator of a corporation's profitability.

price index *n.* A number relating prices of a group of commodities to their prices during an arbitrarily chosen base period.

price·less (prīs'lĭs) *adj.* 1. Of inestimable worth: INVALUABLE. 2. Highly amusing, absurd, or odd.

price tag *n.* 1. A label on a piece of merchandise showing its price. 2. Cost: price.

price war *n.* A period of sharp competition among businesses in which each competitor tries to cut retail prices below those of the others.

pric·ey (prī'sē) *adj.* **-i·er, -i·est.** *Informal.* Expensive.

prick (prĭk) *n.* [ME < OE *prica*, puncture.] 1. a. An act of piercing or pricking. b. The sensation of being pierced or pricked. 2. A painful or stinging feeling of remorse or sorrow. 3. A small mark or puncture made by a pointed object. 4. A hare's track or footprint. 5. A pointed object, as an ice pick or thorn. —*v.* **pricked, prick·ing, pricks.** —*vt.* 1. To puncture lightly. 2. To sting with an emotional or mental pang. 3. To impel: incite <'My duty *pricks* me on' Shakespeare> 4. To mark on a surface by means of small punctures <*prick* a design on leather> 5. *Naut.* To measure with dividers on a chart. 6. To pierce the quick of (a horse's hoof) while shoeing. 7. To transplant (seedlings) before a final planting. —*vi.* 1. To pierce or puncture something. 2. To feel a stinging or pricking sensation. 3. To ride at a gallop. 4. To point upward. **—prick up (one's) ears.** To begin to listen attentively.

prick·er (prĭk'ər) *n.* 1. One that pricks. 2. A pricking tool. 3. A prickle or thorn.

prick·et (prĭk'ĭt) *n.* [ME *priket* < *prik*, prick < OE *prica*, puncture.] 1. a. A small point or spike for holding a candle upright. b. A candlestick with such a spike. 2. A buck in its second year, prior to the branching of its horns.

prick·le (prĭk'əl) *n.* [ME *prikel* < OE *pricel*.] 1. A small sharp point, spine, or thorn. 2. A tingling or pricking sensation. —*v.* **-led, -ling, -les.** —*vt.* 1. To prick with or as if with a thorn. 2. To cause a tingling or pricking sensation in. —*vi.* 1. To feel a tingling or pricking sensation. 2. To stand up like prickles.

prick·ly (prĭk'lē) *adj.* **-li·er, -li·est.** 1. Having prickles. 2. Tingling: smarting. 3. Irritable. **—prick'li·ness** *n.*

prickly ash *n.* An aromatic shrub or small tree, *Zanthoxylum americanum*, of eastern North America, with prickly stems and feathery leaves.

prickly heat *n.* Miliaria.

prickly pear *n.* 1. Any of various cacti of the genus *Opuntia*, with bristly flattened or cylindrical joints, showy, usu. yellow flowers, and ovoid, occas. edible fruit. 2. The fruit of a prickly pear.

prickly poppy *n.* Any of various plants of the genus *Argemone*, chiefly of tropical America, with large yellow or white flowers and prickly leaves, stems, and pods.

pric·ky (prĭk'ē) *adj.* **-i·er, -i·est.** Prickly.

pride (prīd) *n.* [ME < OE *prȳde* < *prūd*, proud < OFr.] 1. A sense of one's own proper value or dignity: SELF-RESPECT. 2. Pleasure or satisfaction taken in one's work, achievements, or possessions. 3. a. A source of pride <These soldiers were their country's *pride*.> b. The most successful or thriving condition: PRIME <the *pride* of youth> 4. a. An overly high opinion of oneself: CONCEIT. b. Consideration or personification of this condition as the first of the seven cardinal sins. 5. Mettle or spirit in horses. 6. A group of lions. —*v.* **prid·ed, prid·ing, prides.** —*vt.* To esteem (oneself) for <I *pride* myself on this cabinetwork.> —*vi.* To indulge in self-esteem. **—pride'ful** *adj.* **—pride'ful·ly** *adv.* **—pride'ful·ness** *n.*

pri·e-dieu (prē-dyœ') *n., pl.* **-dieus** or **-dieux** (-dyœz') [Fr. *prie Dieu*, pray God.] A low desk with space for a book above and with a foot piece below for kneeling in prayer.

pri·er *also* **pry·er** (prī'ər) *n.* One who pries.

priest (prēst) *n.* [ME *preost* < OE *prēost* < VLat. **prester* < LLat. *presbyter*. —see PRESBYTER.] 1. A member of the second grade of clergy ranking below a bishop but over a deacon and having authority to pronounce absolution and administer all sacraments save that of ordination in the Roman Catholic, Eastern Orthodox, Anglican, Armenian, and separated Catholic hierarchies. 2. A non-Catholic cleric. 3. One whose role is considered comparable to that of a priest <computers and their *priests*> —*vt.* **priest·ed, priest·ing, priests.** To ordain or admit to the priesthood. **—priest'hood** *n.*

▲ word history: *Priest* and *presbyter* are both descended from the Greek word *presbuteros*, literally "elder," the comparative form of *presbus*, "old man." The Greek word was used in early Christian writing to denote a particular order of Christian minister. *Presbuteros* was borrowed into Latin and from there it was borrowed into the Germanic languages, appearing in Old English as *prēost*, modern *priest*. Because Old English *prēost* and its descendants were used to

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lateral myocardial i., i. involving only the lateral wall of the heart, producing indicative electrocardiographic changes confined to leads I, aVL, V5, and V6.

myocardial i., cardiac i.; i. of an area of the heart muscle, usually as a result of occlusion of a coronary artery.

myocardial i. in H-form, i. involving the septum along with both inferior and anterior walls to make an H-shaped configuration.

nontransmural myocardial i. (NTMI), necrosis of heart muscle that fails to extend from the endocardium to the epicardium, often erroneously considered benign.

posterior myocardial i., i. involving the posterior wall of the heart; also formerly used of i.'s involving the inferior or diaphragmatic surface of the heart.

silent myocardial i., i. that produces none of the characteristic symptoms and signs of myocardial i.

subendocardial myocardial i., i. that involves only the layer of muscle subjacent to the endocardium.

through-and-through myocardial i., transmural myocardial i.

transmural myocardial i., through-and-through myocardial i.; i. that involves the whole thickness of the heart muscle from endocardium to epicardium.

watershed i., cortical i. in an area of blood supply between two major cerebral arteries.

infect (in-fekt') [L. *in- ficio,* pp. *-fectus,* to dip into, dye, corrupt, infect, fr. *in* + *facio,* to make. FAC-]. 1: To enter, invade, or inhabit another organism, causing infection or contamination. 2. To dwell internally, endoparasitically, as opposed to externally (infestation).

infection (in-fek'shun). Endoparasitism; multiplication of parasitic organisms within the body. Multiplication of bacteria of the "normal" flora of the intestinal tract is not usually viewed as being an i., whereas multiplication of other organisms; *e.g., Vibrio cholerae,* is so viewed.

agonal i., terminal i.

apical i., the implantation of a microorganism at the apex of a tooth; usually the result of the migration of a microorganism from the pulp canal through the apical foramen.

cross i., i. spread from one source to another, person to person, animal to person, person to animal, animal to animal.

cryptogenic i., bacterial, viral, or other i., the source of which is unknown.

droplet i., i. acquired through the inhalation of droplets or aerosols of saliva or sputum containing virus or other microorganisms expelled by another person during sneezing, coughing, laughing, or talking.

endogenous i., i. caused by an infectious agent already present in the body, the previous i. having been inapparent.

focal i., an old term which distinguishes local i.'s (focal) from generalized i.'s (sepsis).

latent i., an asymptomatic i. capable of manifesting symptoms under particular circumstances; *e.g.,* stress.

mass i., i. resulting from the entrance of a large number of pathogens into the circulation or tissues.

mixed i., i. by more than one variety of pathogenic microorganisms.

pyogenic i., i. characterized by local pus formation or pyemia, caused by one of the pyogenic bacteria (staphylococcus, streptococcus, pneumococcus, meningococcus, or *Haemophilus influenzae).*

secondary i., an i., usually septic, occurring in a person or animal already suffering from an i. of another nature.

staphylococcal i., staphylococcemia.

streptococcal i., streptococcemia.

superficial scalp i., an i. external to the galea; *e.g.,* folliculitis or cellulitis.

terminal i., agonal i.; an acute i., commonly pneumonic or septic, occurring toward the end of any disease (usually a chronic disease), and often the cause of death.

Vincent's i., necrotizing ulcerative *gingivitis.*

zoonotic i., an i. shared in nature by man with other species of vertebrate animals.

infection-immunity. See under immunity.

infectiosity (in-fek-shī-os'ī-tī). Infectiousness.

infectious (in-fek'shus). 1. Capable of being transmitted by infection, with or without actual contact (see also contagious). 2. Infective. 3. Denoting a disease due to the action of a microorganism.

infec'tive. Infectious (2); producing or relating to an infection.

infecundity (in-fe-kun'dī-tī) [L. *infecunditas,* barrenness]. Sterility in woman; barrenness.

inferior (in-fe'rī-or) [L. lower]. 1: Situated below or directed downward. 2 [NA]. In human anatomy, situated nearer the soles of the feet in relation to a specific reference point; opposite of superior.

infe'rior'ity. The condition or state of being or feeling inadequate or inferior, especially to others similarly situated.

in'fertil'ity. [L. *in-* neg. + *fertilis,* fruitful]. Relative sterility; diminished or absent fertility; does not imply (either in the male or the female) the existence of as positive or irreversible a condition as sterility. In the female, it indicates adequate anatomical structures and equivocal function, with the possibility of pregnancy that may or may not proceed to term.

infest (in-fest') [L. *infesto,* pp. *-atus,* to attack]. 1: To infect, usually by macroscopic parasites; to invade parasitically. 2. To occupy a site and dwell ectoparasitically on the external surface, as opposed to dwelling within a host (infection).

infesta'tion. Ectoparasitism; the act or process of infesting.

infiltrate (in-fil'trāt) [L. *in* + Mediev. L. *filtro,* pp. *-atus,* to strain through felt, fr. *filtrum,* felt]. 1: To percolate; to enter or cause to enter the pores of a substance, denoting a liquid. 2. Material that has permeated or infiltrated into the tissues.

Assmann's tuberculous i., infraclavicular i.

infraclavicular i., Assmann's tuberculous i.; an incipient lesion of tuberculous infection.

infiltration (in'fil-tra'shun). 1: The act of passing into or interpenetrating a substance, cell, or tissue; said of gases, fluids, or matters held in solution. 2. The gas, fluid, or dissolved matter that has entered any substance, cell, or tissue.

adipose i., growth of normal adult fat cells in sites where they are not usually present.

calcareous i., calcification.

cellular i., migration of cells from their sources of origin, or direct extension of cells as a result of unusual growth and multiplication, thereby resulting in fairly well defined foci, irregular accumulations, or diffusely distributed individual cells in the connective tissue and interstices of various organs and tissues; used especially with reference to such changes associated with inflammations and certain types of malignant neoplasms.

epituberculous i., an i. superimposed upon a tuberculous lesion.

fatty i., abnormal accumulation of fat droplets in the cytoplasm of cells, particularly of fat derived from outside the cells. See also fatty *degeneration.*

gelatinous i., gray i.

gray i., gelatinous i.; a term sometimes used for the relatively rapidly formed, semisolid, gray or gray-white exudate (chiefly necrotic cells and remnants of tissue, and macrophages) resulting from unusually acute, overwhelming, diffuse tuberculous infection in the lung.

paraneural i., i. around a nerve.

infin'ity. See infinite *distance.*

infirm (in-firm') [L. *in- firmus,* fr. *in-* neg. + *firmus,* strong]. Weak or feeble because of old age or disease.

infirmary (in-fir'mă-rī) [L. *infirmarium;* see infirm]. A small hospital, especially in a school or college.

infirmity (in-fir'mī-tī). A weakness; an abnormal, more or less disabling, condition of mind or body.

inflam'mable [L. *in-* + *flamma,* flame]. Flammable.

inflammation (in-flă-ma'shun) [L. *inflammo,* pp. *-atus,* fr. *in,* in, + *flamma,* flame]. A fundamental pathologic process consisting of a dynamic complex of cytologic and histologic reactions that occur in the affected blood vessels and adjacent tissues in response to an injury or abnormal stimulation caused by a physical, chemical, or biologic agent, including (1) the local reactions and resulting morphologic changes, (2) the destruction or removal of the injurious material, and (3) the responses that lead to repair